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In the Claims

Please amend the claims pursuant to the provisions of 37 C.F.R. § 1.121, as follows:

1. (currently amended) A compound having the formula:

H1-Y-H2

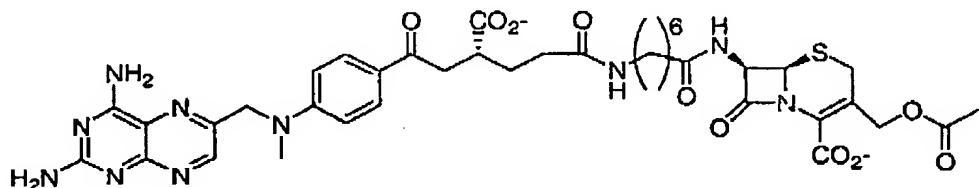
wherein H1 is a substrate capable of selectively binding to a first receptor;

wherein H2 is a substrate capable of selectively binding to and selectively forming a covalent bond with a ~~second receptor~~ the penicillin binding protein ("PBP") or with the thymidine synthase ("TS") enzyme; and

wherein Y is a moiety providing a covalent linkage between H1 and H2, which may be present or absent, and when absent, H1 is covalently linked to H2.

2.-4. (canceled)

5. (currently amended) The compound of claim 2 1 having the structure:



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6.-14. (canceled)

15. (previously presented) A cell comprising a DNA sequence which on transcription gives rise to a first fusion protein exogenous to the cell and a second fusion protein exogenous to the cell,

wherein the first fusion protein is a receptor domain fused with a DNA-binding domain; and

wherein the second fusion protein is a transcription activation domain fused to either a penicillin-binding-protein ("PBP") or to a thymidine synthase ("TS") enzyme.

16. (previously presented) The cell of claim 15, wherein the receptor domain of the first fusion protein is DHFR.

17. (previously presented) The cell of claim 15, wherein the DNA-binding domain of the first fusion protein is LexA.

18. (previously presented) The cell of claim 15, wherein the transcription activation domain of the second fusion protein is B42.

19. (previously presented) The cell of claim 15, wherein the PBP is the *Streptomyces* R61 PBP.

20. (previously presented) The cell of claim 15, wherein the first fusion protein is eDHFR-LexA, and the second fusion protein is R61-B42.

21. (previously presented) The cell of claim 15, where the

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cell is a yeast cell, a bacteria cell or a mammalian cell.

22. (previously presented) The cell of claim 15, where the cell is *S. cerevisiae* or *E. coli*.

23.-29. (canceled)

30. (previously presented) A method for identifying a molecule that binds a known target in a cell from a pool of candidate molecules, comprising:

- (a) forming a screening molecule by covalently bonding each molecule in the pool of candidate molecules to a substrate capable of selectively binding to and selectively forming a covalent bond with a receptor;
- (b) introducing the screening molecule into a cell culture comprising cells that express
 - a first fusion protein of a DNA-binding domain fused to a known target receptor domain against which the candidate molecule is screened,
 - a second fusion protein which comprises a receptor domain capable of binding to and forming a covalent bond with the screening molecule, and
 - a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;
- (c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein, bringing the two fusion proteins in to proximity so as to activate the expression of the reporter gene;
- (d) selecting the cell that expresses the reporter gene;

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and

(e) identifying the small molecule that binds the known target receptor.

31. (previously presented) The method of claim 30, wherein the cell is selected from the group consisting of insect cells, yeast cells, mammalian cells, and their lysates.

32. (previously presented) The method of claim 30, wherein the DNA-binding domain of the first fusion protein is LexA.

33. (previously presented) The method of claim 30, wherein the transcription activation domain of the second fusion protein is B42.

34. (previously presented) The method of claim 30, wherein the receptor domain of the second fusion protein is a penicillin-binding-protein ("PBP") or to a thymidine synthase ("TS") enzyme.

35. (previously presented) The method of claim 34, wherein the PBP is the *Streptomyces* R61 PBP.

36. (previously presented) The method of claim 30, wherein the molecule is obtained from a combinatorial library.

37. (previously presented) The method of claim 30, wherein the steps (b)-(e) of the method are iteratively repeated in the presence of a preparation of random small molecules for competitive binding with the screening molecule so as to

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identify a molecule capable of competitively binding the known target receptor.

38. (previously presented) A method for identifying an unknown target receptor to which a molecule is capable of binding in a cell, comprising:

- (a) providing a screening molecule having a ligand which has a specificity for the unknown target receptor covalently bonded to a substrate capable of selectively binding to and selectively forming a covalent bond with a receptor;
- (b) introducing the screening molecule into a cell which expresses

a first fusion protein of a DNA-binding domain fused to the unknown target receptor domain against which the candidate molecule is screened,

a second fusion protein which comprises a receptor domain capable of binding to and forming a covalent bond with the screening molecule, and

a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

- (c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene;
- (d) selecting which cell expresses the unknown target receptor; and

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(e) identifying the unknown target receptor.

39. (previously presented) The method of claim 38, wherein the unknown protein target is encoded by a DNA from the group consisting of genomicDNA, cDNA and syntheticDNA.

40. (previously presented) The method of claim 38, wherein the ligand has a known biological function.

41.-54. (canceled)

55. (new) A method for screening a cDNA library by identifying the expressed protein target, comprising:

- (a) providing a screening molecule comprising a methotrexate moiety covalently bonded to a ligand which has a known specificity;
- (b) introducing the screening molecule into a cell which expresses a first fusion protein comprising a binding domain capable of binding methotrexate, a second fusion protein comprising the expressed unknown protein target, and a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;
- (c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene;
- (d) selecting which cell expresses the reporter gene; and

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(e) identifying the unknown protein target and the corresponding cDNA.

56. (new) The method of claim 55, wherein the unknown protein target is encoded by a DNA from the group consisting of genomicDNA, cDNA and syntheticcDNA.